

Effect of substrate stiffness on early mouse embryo development.

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Public Summary:

It is becoming increasingly clear that cells are remarkably sensitive to the biophysical cues of their microenvironment and that these cues play a significant role in influencing their behaviors. In this study, we investigated whether the early pre-implantation embryo is sensitive to mechanical cues, i.e. the elasticity of the culture environment. To test this, we have developed a new embryo culture system where the mechanical properties of the embryonic environment can be precisely defined. The contemporary standard environment for embryo culture is the polystyrene petri dish (PD), which has a stiffness (1 GPa) that is six orders of magnitude greater than the uterine epithelium (1 kPa). To approximate more closely the mechanical aspects of the in vivo uterine environment we used polydimethyl-siloxane (PDMS) or fabricated 3D type I collagen gels (1 kPa stiffness, Col-1k group). Mouse embryo development on alternate substrates was compared to that seen on the petri dish; percent development, hatching frequency, and cell number were observed. Our results indicated that embryos are sensitive to the mechanical environment on which they are cultured. Embryos cultured on Col-1k showed a significantly greater frequency of development to 2-cell ($68 \pm 15\%$ vs. $59 \pm 18\%$), blastocyst ($64 \pm 9.1\%$ vs. $50 \pm 18\%$) and hatching blastocyst stages ($54 \pm 25\%$ vs. $21 \pm 16\%$) and an increase in the number of trophectodermal cell (TE, 65 ± 13 vs. 49 ± 12 cells) compared to control embryos cultured in PD (mean \pm S.D.; $p < .01$). Embryos cultured on Col-1k and PD were transferred to recipient females and observed on embryonic day 12.5. Both groups had the same number of fetuses, however the placentas of the Col-1k fetuses were larger than controls, suggesting a continued effect of the preimplantation environment. In summary, characteristics of the preimplantation microenvironment affect pre- and post-implantation growth.

Scientific Abstract:

It is becoming increasingly clear that cells are remarkably sensitive to the biophysical cues of their microenvironment and that these cues play a significant role in influencing their behaviors. In this study, we investigated whether the early pre-implantation embryo is sensitive to mechanical cues, i.e. the elasticity of the culture environment. To test this, we have developed a new embryo culture system where the mechanical properties of the embryonic environment can be precisely defined. The contemporary standard environment for embryo culture is the polystyrene petri dish (PD), which has a stiffness (1 GPa) that is six orders of magnitude greater than the uterine epithelium (1 kPa). To approximate more closely the mechanical aspects of the in vivo uterine environment we used polydimethyl-siloxane (PDMS) or fabricated 3D type I collagen gels (1 kPa stiffness, Col-1k group). Mouse embryo development on alternate substrates was compared to that seen on the petri dish; percent development, hatching frequency, and cell number were observed. Our results indicated that embryos are sensitive to the mechanical environment on which they are cultured. Embryos cultured on Col-1k showed a significantly greater frequency of development to 2-cell ($68 \pm 15\%$ vs. $59 \pm 18\%$), blastocyst ($64 \pm 9.1\%$ vs. $50 \pm 18\%$) and hatching blastocyst stages ($54 \pm 25\%$ vs. $21 \pm 16\%$) and an increase in the number of trophectodermal cell (TE, 65 ± 13 vs. 49 ± 12 cells) compared to control embryos cultured in PD (mean \pm S.D.; $p < .01$). Embryos cultured on Col-1k and PD were transferred to recipient females and observed on embryonic day 12.5. Both groups had the same number of fetuses, however the placentas of the Col-1k fetuses were larger than controls, suggesting a continued effect of the preimplantation environment. In summary, characteristics of the preimplantation microenvironment affect pre- and post-implantation growth.